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"Signaling From Irradiated To Non-Irradiated Cells".

[Transmission of cancer causing signals from irradiated to non-irradiated cells.]

The overall objective of this proposal is to define the effects of low doses of ionizing radiation in human cells with particular emphasis on effects in bystander cells that do not receive a direct radiation exposure and in their progeny. It focuses on quantifying the risk of transfonnation of nonnal cells into cancer cells upon exposure to low doses of alpha- particle radiation such as from radon gas. Under such radiation conditions, only a very small fraction of the cells in an exposed population will be irradiated.
Radon gas occurs naturally in the environment and is present at high concentrations in underground mines where it has been conclusively shown to cause lung cancer. Radon is also present in homes raising concern that it increases lung cancer risk for the general population. Based on effects observed at high doses, it is estimated that 10-14% of all lung cancers in the US may be linked to radon gas in the environment. However, these estimates may be biased by confounding factors such as smoking and age. Therefore, detennination of the cellular effects of low doses of radiation in stringently controlled laboratory experiments will contribute to the fonnulation of adequate guidelines to protect the public from cancer caused by indoor radon. Currently, our knowledge of the harmful effects of alpha-particle radiation is limited. However, recent evidence indicates that bystander non-irradiated cells neighboring those cells traversed by alpha-particles sustain significant damage to their DNA, the blueprint that detennines their fate. However, it is unknown whether the genetic changes in bystander cells result in their transfonnation into cancer cells and whether the induced changes are transmitted to their progeny. The proposed studies based on the hypothesis that "traversal of radiation through a cell produces measurable damage in neighboring bystander cells and leads to their transformation into cancer cells" aim at studying these effects. They willl) Measure the frequency of transfonnation of normal cells into cancer cells in populations of cells exposed to very low doses of alpha particles. Detennine the role of intercellular communication in the transmission of cancer causing signals from irradiated to bystander cells. 2) Determine the long- term consequences of biological effects in bystander human and rodent cells that have been identified and isolated from cell populations where they co-existed with cells containing radiation-emitting compounds. Examine the persistence of DNA damage and the propensity to transfonn to the cancer-state in the descendants of directly irradiated and bystander cells. These studies are significant to radiation and environmental protection and to diagnostic and therapeutic medicine protocols that use radiation-emitters to detect and treat cancer .